

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/02450

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/415 A61K39/35 G01N33/68 C12N15/82 A01H5/10  
A23L1/025

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, PAJ, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/25793 A (HILL ADRIAN VIVIAN SINTON ; ISIS INNOVATION (GB); ANDERSON ROBERT P) 12 April 2001 (2001-04-12) cited in the application	1-5, 11, 13-19, 25-42, 44-64, 67-84
Y	page 1-20; claims 1-59; figures 12G, 14-28; examples 3, 8; tables 7-9	6-10, 20-24, 43, 65
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

7 June 2004

Date of mailing of the international search report

0 9. 07. 04

Name and mailing address of the ISA

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PIPER JUSTIN L ET AL: "High selectivity of human tissue transglutaminase for immunoactive gliadin peptides: Implications for Celiac Sprue" BIOCHEMISTRY, vol. 41, no. 1, 8 January 2002 (2002-01-08), pages 386-393, XP002267668 ISSN: 0006-2960 Abstract, Introduction, Discussion	28,30, 32-34
Y	the whole document	1-11, 13-27, 44-58, 60-64,67
X	ARENTZ-HANSEN H ET AL: "THE INTESTINAL T CELL RESPONSE TO ALPHA-GLIADIN IN ADULT CELIAC DISEASE IS FOCUSED ON A SINGLE DEAMIDATED GLUTAMINE TARGETED BY TISSUE TRANSGLUTAMINASE" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 191, no. 4, 21 February 2000 (2000-02-21), pages 603-612, XP000986723 ISSN: 0022-1007 cited in the application Abstract, Table II, Fig.4, Discussion	28,30, 32-34
Y		44-58, 60-64,67
X	ANDERSON R P ET AL: "IN VIVO ANTIGEN CHALLENGE IN CELIAC DISEASE IDENTIFIES A SINGLE TRANSGLUTAMINASE-MODIFIED PEPTIDE AS THE DOMINANT A-GLIADIN T-CELL EPITOPE" NATURE MEDICINE, NATURE AMERICA, NEW YORK, US, vol. 6, no. 3, March 2000 (2000-03), pages 337-342, XP000982628 ISSN: 1078-8956 abstract; figure 1	28,30, 32-34
Y		44-58, 60-64,67
X	EP 0 905 518 A (UNIV LEIDEN ;ACADEMISCH ZIEKENHUIS LEIDEN (NL)) 31 March 1999 (1999-03-31)  Paragr. '0001!-'0014!; SEQ ID NOs:11,12,14,15,16 claims 11-14; figures 3,5	1-11, 13-28, 30, 32-34, 44-58, 60-64,67
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	VADER L W ET AL: "Specificity of tissue transglutaminase explains cereal toxicity in celiac disease" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 195, no. 5, 4 March 2002 (2002-03-04), pages 643-649, XP002204499 ISSN: 0022-1007 cited in the application Abstract, Page 645, Figure 1	1-11, 13-28, 30, 32-34, 44-58, 60-64,67
Y	WIESER H ET AL: "COELIAC ACTIVE PEPTIDES FROM GLIADIN: LARGE-SCALE PREPARATION AND CHARACTERIZATION" ZEITSCHRIFT FUER LEBENSMITTELUNTERSUCHUNG UND -FORSCHUNG, XX, XX, vol. 194, no. 3, 1992, pages 229-234, XP002072056 ISSN: 0044-3026 Summary; sequence B3143	1-11, 13-28, 30, 32-34, 44-58, 60-64,67
Y	KUMAR R ET AL: "Human Genome Search in Celiac Disease: Mutated Gliadin T-cell-like Epitope in Two Human Proteins Promotes T-cell Activation" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 319, no. 3, 30 May 2002 (2002-05-30), pages 593-602, XP004449660 ISSN: 0022-2836 Abstract; pages 597-599	12,29, 31-33, 35-42, 59,64, 68-84
Y	& KUMAR ET AL: "Human Genome Search in Celiac Disease: Mutated Gliadin T-cell-like Epitope in Two Human Proteins Promotes T-cell Activation" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, 'Online! 30 May 2002 (2002-05-30), doi:10.1016/S0022-2836(02)00366-2 Retrieved from the Internet: <URL:www.sciencedirect.com> 'retrieved on 2004-06-01!	
Y	MOUSTAKAS A K ET AL: "STRUCTURE OF CELIAC DISEASE-ASSOCIATED HLA-DQ8 AND NON-ASSOCIATED HLA-DQ9 ALLELES IN COMPLEX WITH TWO DISEASE-SPECIFIC EPITOPES" INTERNATIONAL IMMUNOLOGY, OXFORD UNIVERSITY PRESS, GB, vol. 12, no. 8, August 2000 (2000-08), pages 1157-1166, XP001021489 ISSN: 0953-8178 the whole document	12,29, 31-33, 35-42, 59,64, 68-84

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JUNG G ET AL: "From combinatorial libraries to MHC ligand motifs, T-cell superagonists and antagonists" BIOLOGICALS, ACADEMIC PRESS LTD., LONDON, GB, vol. 29, no. 3-4, September 2001 (2001-09), pages 179-181, XP002242277 ISSN: 1045-1056 the whole document	12,29, 31-33, 35-42, 59,64, 68-84
Y	MOWAT A M: "Coeliac disease-a future for peptide therapy?" LANCET, XX, XX, vol. 356, no. 9226, 22 July 2000 (2000-07-22), pages 270-271, XP004263756 ISSN: 0140-6736  the whole document	1,2,4-7, 9-11, 13-16, 18-21, 23-28, 30, 32-34, 44-58, 60-64,67
Y	MADSEN LARS S ET AL: "A humanized model for multiple sclerosis using HLA-DR2 and a human T-cell receptor" NATURE GENETICS, vol. 23, no. 3, November 1999 (1999-11), pages 343-347, XP002283438 ISSN: 1061-4036 the whole document	43,65
A	O'KEEFFE J ET AL: "T CELL PROLIFERATION, MHC CLASS II RESTRICTION AND CYTOKINE PRODUCTS OF GLIADIN-STIMULATED PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMC)" CLINICAL AND EXPERIMENTAL IMMUNOLOGY, OXFORD, GB, vol. 117, no. 2, August 1999 (1999-08), pages 269-276, XP000989621 ISSN: 0009-9104 the whole document	
A	WAL VAN DE Y ET AL: "Coeliac disease: it takes three to tango " GUT, BRITISH MEDICAL ASSOCIATION, LONDON,, GB, vol. 46, 2000, pages 734-737, XP002204498 ISSN: 0017-5749	

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/02450

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	ARENTZ-HANSEN HELENE ET AL: "Celiac lesion T cells recognize epitopes that cluster in regions of gliadins rich in proline residues" GASTROENTEROLOGY, vol. 123, no. 3, September 2002 (2002-09), pages 803-809, XP009024146 ISSN: 0016-5085  abstract; table 1 ---	1,2,4-7, 9-11, 13-16, 18-21, 23-28, 30, 32-34, 44-58, 60-64,67
Y,P	WO 02/083722 A (KONING FRITS ;ACADEMISCH ZIEKENHUIS LEIDEN (NL); DRIJFHOUT JAN WOU) 24 October 2002 (2002-10-24) page 1-15; claims 1-52 ---	1
E	WO 03/066079 A (KONING FRITS ;ACADEMISCH ZIEKENHUIS LEIDEN (NL); DRIJFHOUT JAN WOU) 14 August 2003 (2003-08-14) & EP 1 332 760 A (ACADEMISCH ZIEKENHUIS LEIDEN) 6 August 2003 (2003-08-06) SEQ ID NOs: 2,21,38,42,43,46,59,73 figure 2B ---	1-11
E	WO 03/096984 A (HAUSCH FELIX ;QUARSTEN HANNE (NO); SOLLID LUDVIG M (NO); UNIV LELA) 27 November 2003 (2003-11-27)  page 1-18; claims 1-18 -----	12,29, 31-33, 35-42, 59,64, 68-84

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## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-14: 67  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 66  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 1-14; 67

Although claims 1-14 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the agent.  
Although claim 67 is directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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Continuation of Box I.2

Claims Nos.: 66

Present claim 66 relates to a product defined by reference to a method of identification having the desirable characteristic of being of use in a method of preventing or treating coeliac disease.

The claim covers all products having this characteristic, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the products mentioned in Table 9 of the description.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-2, 4-7, 9-11, 13-16, 18-21,  
23-28, 30, 32-34, 44-58, 60-64, 67, all partially

All embodiments concerning in particular the closely related wheat sequences SEQ ID NOS:18-20, 31 and 34-35, HLA-DQ2-restricted.

Invention 2: claims 1-2, 4-7, 9-11, 13-16, 18-21,  
23-28, 30, 32-34, 44-58, 60-64, 67, all partially

All embodiments concerning in particular the closely related wheat sequences SEQ ID NOS:21-22, 42, 43 and 46, HLA-DQ2-restricted.

Invention 3: claims 1-2, 4-7, 9-11, 13-16, 18-21,  
23-28, 30, 32-34, 44-58, 60-64, 67, all partially

All embodiments concerning in particular the wheat sequences SEQ ID NOS:32-33 and 36, HLA-DQ2-restricted.

Invention 4: claims 1-4, 6-11, 13-16, 18, 20-28,  
30, 32-34, 44-58, 60-64, 67, all partially

All embodiments concerning in particular the rye secalins and barley hordeins SEQ ID NOS:39-41, HLA-DQ2-restricted.

Invention 5: claims 1, 3-11, 13-15, 17-28, 30,  
32-34, 44-58, 60-64, 67, all partially

All embodiments concerning in particular the epitope SEQ ID NO:44 bioactive in HLA-DQ8+ patients.

Invention 6: claims 12, 29, 31, 35-42, 59, 68-84,  
completely; claims 32-33, 64, partially

All embodiments referring to antagonists or mutated gliadin proteins.

Invention 7: claims 43, 65-66



FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

Concerning mammals expressing a T cell receptor that  
recognises a peptide.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/02450

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0125793	A	12-04-2001	AU 7539400 A CA 2386089 A1 EP 1218751 A2 WO 0125793 A2 JP 2003511670 T	10-05-2001 12-04-2001 03-07-2002 12-04-2001 25-03-2003
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WO 02083722	A	24-10-2002	CA 2443886 A1 EP 1377604 A2 WO 02083722 A2 NO 20034588 A	24-10-2002 07-01-2004 24-10-2002 10-12-2003
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WO 03096984	A	27-11-2003	WO 03068170 A2 WO 03096979 A2 WO 03096984 A2 US 2003215438 A1	21-08-2003 27-11-2003 27-11-2003 20-11-2003